

REMARKS

The Amendments

Claim 1 is amended to incorporate the substance of previous claims 5 and 26 therein; see also, page 3, lines 1-2; page 4, lines 11-13; and Example 1. Claims 5 and 26 are, accordingly, canceled. Claims 9 and 10 are amended to correct a minor informality by providing consistent use of terms and proper Markush language. It is clarified that the UV filter is in addition to isoquercetin. The claim 9 and 10 amendments do not change the scope of these claims.

It is submitted that the above amendments would put the application in condition for allowance or materially reduce or simplify the issues for appeal. The amendments do not raise new issues or present new matter since they merely incorporate already examined dependent claim recitations into the independent claims. No additional claims are presented. Although applicants do not believe the amendments were necessary to distinguish the prior art, they have been made to provide an even greater distinction in the hopes of furthering the prosecution of this application. They were not earlier presented because it was not previously believed further amendment of the claims was needed. Also, they were made in light of a new ground of rejection being made in the Final Office Action. Accordingly, it is submitted that it is proper to present these amendments after the Final rejection and that the requested amendments should be entered.

To the extent that the amendments avoid the prior art or for other reasons related to patentability, competitors are warned that the amendments are not intended to and do not limit the scope of equivalents which may be asserted on subject matter outside the literal scope of any patented claims but not anticipated or rendered obvious by the prior art or

otherwise unpatentable to applicants. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Obviousness-type Double Patenting Rejection

The rejection of claims 1, 4-5, 7-10, 13-14 and 26 for obviousness-type double patenting over claims 1-24 of U.S. Patent No. 6,491,948 is respectfully traversed.

Applicants have never argued that the instant claims exclude compositions which contain ascorbic acid or a derivative thereof. Applicants argument was that the instant claims do not require an ascorbic acid component, whereas, the '948 patent claims do require an ascorbic acid component as an essential feature. On the other hand, the instant claims require a second component which is 5-ethyldeoxyuridine, galangin, propolis, chrysin, apigenin, luteolin, acacetin, eriodictyol, quercitrin, catechol, hesperitin, a glycoside of any of the above other components, or a carotene, and the '948 claims require no such component. Clearly, the instant claims and the '948 claims both do require isoquercetin/isoquercitrin. But one common required component together with the open "comprising" transition term does not support the position that the claims are directed to obvious variants of the same invention where they each require a second component which is distinct from the other.

If the current rejection were proper, then it would follow that any claim drawn to a chemical composition "comprising" a component A would provide the basis for obviousness-type double patenting over every claim directed to a chemical composition "comprising" any component B, whether component B is novel or not. The claim to a composition comprising component A does not exclude compositions which comprise component B. Thus, under the reasoning of the Office Action, obviousness-type double patenting would exist. But this is

clearly not a correct application of obviousness-type double patenting. If this were a correct application, then nearly every open-ended patent claim would provide a basis for obviousness-type double patenting over nearly every other open-ended patent claim. The fact that the claims here have one component in common does not change the issue.

Obviousness-type double patenting is only applicable where an applicant is trying to obtain two claims directed to the same "invention" or an obvious variant thereof. The "invention" in the instant claims is the combination of isoquercitrin (in the amount recited) with the second component (not inclusive of ascorbic acid). The "invention" in the '948 patent is the combination of isoquercetin with a second component which is an ascorbic acid component. The clear distinction of the second components dictates that the combinations to which the "inventions" are drawn are also clearly distinct, i.e., not obvious variants of one another.

Accordingly, applicants urge that the instant claims which do not require an ascorbic acid component but do require the discussed second component cannot be obvious variants of the patented claims which do require an ascorbic acid component but make not mention or suggestion of a component meeting applicants' second component. Thus, the obviousness-type double patenting rejection should be withdrawn.

The Rejections under 35 U.S.C. §103

The rejections of claims 1, 4-5, 7-10, 13-14 and 26 under 35 U.S.C. §103, as being obvious over Abou-Karam (J.Nat.Prod.) in view of Bean (U.S. Patent No. 4,132,782), or further in view of Lanzendorfer (WO 96/18381) are respectfully traversed.

Abou-Karam provides a brief disclosure that isoquercitrin has some, unquantified, antiviral action against herpes simplex type 1 virus. The amounts mentioned for anti-viral

activity in the reference are 40 µg/ml and 250 µg/ml. Assuming a primarily water solution, these would translate to 0.004% and 0.025% by weight of isoquercitrin.

Abou-Karam fails to teach or suggest compositions containing isoquercitrin having antiviral activity which:

- also contain a second component selected from the group consisting of: 5-ethyldeoxyuridine, galangin, propolis, chrysin, apigenin, luteolin, acacetin, eriodictyol, quercitrin, catechol, hesperitin, a glycoside of any of the above other components, and a carotene;
- contain isoquercitrin in an amount of 0.1 - 10% by weight of the composition; and
- are effective as a UV filter; and
- exclude flavones, flavonoids or glycosides thereof other than isoquercitrin or the second component.

Bean teaches the use of an isopropanol extract of mountain ash berry for suppressing herpes simplex virus. The extract composition of Bean contains isoquercitrin and β-carotene but also contains other ingredients, including various flavonols (flavonols are a type of flavonoid); see, e.g., col. 2, lines 10-20. It is admitted in Bean that it is not known what component(s) of the extract give the composition its desired properties. Thus, the reference provides no motivation to one of ordinary skill in the art to isolate any of the components, including isoquercitrin, from any of the other components.

Looking at the combined teachings of Abou-Karam and Bean, one of ordinary skill in the art would be motivated to isolate the isoquercitrin component from the Bean extract for use as an anti-viral against HSV-1. However, there would be no motivation from the combined teachings to isolate the combination of isoquercitrin and β-carotene from the other

flavones, flavonoids or glycosides thereof in the Bean extract. The combined teachings of the references fail to suggest any activity or advantage of β -carotene as an antiviral or anti-herpes agent or any advantage to its combination with isoquercitrin. Thus, there would be no motivation to combine only β -carotene from the Bean extract with isoquercitrin. The Bean extract, itself, is not within the claimed compositions since the claimed compositions exclude flavones, flavonoids or glycosides thereof other than isoquercitrin and the second component. There is no motivation from the prior art to modify the Bean extract by removing all the flavones, flavonoids or glycosides thereof other than isoquercitrin, but retain the β -carotene.

Regarding the counter-arguments in the Final Office Action, applicants take exception to the initial accusation in the Office Action that applicants have merely attacked the references individually. Any proper review of applicants' previous arguments (and those here) would immediately make clear that applicants addressed the combined teachings of the references. Of course the references were discussed individually but that discussion was immediately followed by an analysis of what their combined teachings suggested to one of ordinary skill in the art. To quote some examples from applicants' previous response:

"Looking at the combined teachings of Hovi and Bean, one of ordinary skill in the art would be motivated to isolate the isoquercitrin component from the Bean extract. However, there would be no motivation from the combined teachings to isolate the combination of isoquercitrin and β -carotene from the other flavones, flavonoids or glycosides thereof in the Bean extract. The references fail to suggest any activity or advantage of β -carotene as an antiviral or anti-herpes agent, thus, there would be no motivation to combine only β -carotene from the Bean extract with isoquercitrin."

"Accordingly, it is urged that the combined teaching of Abou-Karam, Hovi and Bean ..."

And

"Lanzendorfer fails to make up for the deficiencies of the combined teachings of the other references to teach combining isoquercitrin with another particular component."

The accusation that applicants did not apply the proper and well-known standard in conducting the 35 U.S.C. §103 analysis should not be made lightly. It amounts to an accusation against applicants and the undersigned that they are incompetent as to the basic legal analysis standards. If the PTO is to maintain this accusation, it is strongly urged that detailed explanation of the basis for this accusation be provided since it appears clear on the record that applicants did use the proper standard by analyzing what the combined teachings of the references suggested to one of ordinary skill in the art.

A further counter-argument in the Final Office Action is that Abou-Karam confirms the anti-viral activity of isoquercitrin against HSV-1 and Bean teaches that "isoquercitrin can be combined together for anti-viral activities. Thus, their combined teachings provide for all elements of the instant compositions." Applicants submit that this is an oversimplification of the issue and does not address all elements of applicants' claims. Bean teaches the combination of isoquercitrin with other components only because Bean had no idea which component had the anti-viral activity. When the proper analysis is made by looking at the combined teachings of the references, as a whole, it is clear that the isoquercitrin was the active component. Thus, considering all the teachings of the prior art, one of ordinary skill in the art would only have been motivated to purify the Bean compositions by isolating isoquercitrin. There is absolutely no suggestion from the references to remove only some of the components of the Bean mixture at col. 2, lines 13-20, and retain some other components. Particularly, there is no suggestion to retain the isoquercitrin and the β -carotene but remove all other flavones, flavonoids or glycosides thereof. Compare instant claim 1. In the absence

of any motivation to one of ordinary skill in the art to make such selective isolation of the components in Bean or to select only certain components from Bean to combine in the Abou-Karam composition, the claimed invention is not suggested by the combined prior art teachings.

Furthermore, the combined teachings of Abou-Karam and Bean fail to provide any teachings at all regarding a composition containing an amount of 0.1 - 10% by weight of isoquercitrin. Abou-Karam's only teachings regarding the amount of isoquercitrin are of much lower amounts and Bean teaches nothing regarding the amount of isoquercitrin in its compositions.

Additionally, the combined teachings of Abou-Karam and Bean fail to provide any teachings at all regarding effectiveness of their compositions as a UV filter.

For all of these reasons, it is urged that the combined teachings of Abou-Karam and Bean fail to render the claimed invention obvious to one of ordinary skill in the art and the rejection under 35 U.S.C. §103, based on the combination of these two references should be withdrawn.

The additional rejection combining the teachings of Lanzendorfer with the above references also does not render the claimed invention obvious to one of ordinary skill in the art. Lanzendorfer provides a very broad teaching of compositions containing multiple types of components and a vast scope of particular components within each type of component. As recognized in the Office Action, Lanzendorfer has no teachings specific to isoquercitrin or its combination with other specific components. Thus, applicants re-iterate that Lanzendorfer fails to make up for the deficiencies of the combined teachings of the other references. Looking at the teachings of all the references, as a whole, one of ordinary skill in the art is not motivated to combine isoquercitrin with another particular component selected from

applicants' listed second components and also to exclude other flavones, flavonoids or glycosides thereof. Lanzendorfer merely provides a laundry list of compounds that have been used to skin ailments and fails to provide any suggestion of the particular combination of components and exclusion of other components which is required to arrive at applicants' claimed compositions.

The legal framework and patent practice discussed in the cited MPEP 2144.05-2144.06 sections also does not support the rejection here. The discussion in MPEP 2144.05 relates to optimization of variables recognized by the prior art as being result-effective variables. It indicates only that there may be a suggestion for optimization of those variables when the prior art provides a generically encompassing teaching of those variables. But there is no generically encompassing teaching here. The references fail to provide any specific or generic teaching regarding the particular combining of components of applicants' invention, while excluding certain other components. There is also no generic teaching as to the amount of isoquercitrin as recited in the instant claims. The optimization case law does not stand for the proposition that variables can be optimized to values outside the range that the prior art suggests. The 2144.06 section of the MPEP discusses the obviousness of combining two components known for the same use to produce that same effect. But the applicability here is not seen. None of the references teach the applicability of "5-ethyldeoxyuridine, galangin, propolis, chrysin, apigenin, luteolin, acacetin, eriodictyol, quercitrin, catechol, hesperitin, a glycoside of any of the above other components, or a carotene" as an anti-viral against Herpesviridae. Further, as already discussed, the references fail to teach such combination to the exclusion of other components, as recited in the instant claims.

The Final Office Action alleges that Lanzendorfer "merely is used to show what is known in the art about optimizing the formulation and concentrations or ingredients in topical

formulations when used in combination with flavonoids." But it must be remembered that the reference has to be considered for its teachings as a whole. Nothing in Lanzendorfer suggests any means of optimizing a composition having the requirements of the instantly claimed compositions.

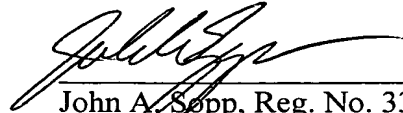
Additionally, Lanzendorfer provides no teachings regarding compositions having any particular amount of isoquercitrin. Further, although Lanzendorfer includes UV filters in its laundry list of possible components, it provides no teaching that isoquercitrin itself is "effective as a UV filter" or could be used in an amount to have such an effect.

For all of the above reasons, it is urged that the combined teachings of Abou-Karam, Bean and Lanzendorfer, considered as a whole, fail to render the claimed invention obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. §103 based thereon should also be withdrawn.

It is submitted that the application is in condition for allowance. But the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



John A. Sopp, Reg. No. 33,103
Attorney/Agent for Applicants

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1
2200 Clarendon Blvd. Suite 1400
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410
Date: February 4, 2005

Attorney Docket No.: MERCK-1900